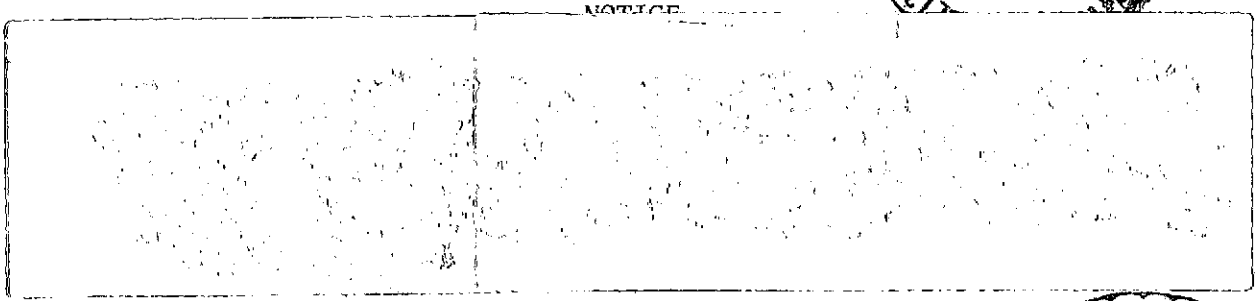
DOES IMMOBILIZATION AND PRESSURE BEARING OF A JOINT RESULT IN OSSIFICATION IN AN ANIMAL EXPERIMENT?

K. Walcher and H. Stuerz

Translation of: "Führt Immobilization und dosierte Druckbelastung eines Gelenkes im Tierversuch zum knochernen Durchbau?" Arch. orthop. Unfall-Chir., Vol. 71, May 1971, pp. 216-247.



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16. Abstract

In an animal experiment the complete immobilization and a pressure bearing applied in doses results in a progressive joint-change which leads to an ossification of the joint if the experiment is extended up to 6 months and the compression on the joint has reached and exceeded the limit of the mechanical pressure capacity of the articular cartilage.

The transfixion of the knee-joint of a rabbit with the aid of a pressure bolt enabled the application of compressions up to 24 kp which produced pressures on the cartilage of up to 120 kp/cm^2. 5 or 6 joints having been exposed to this pressure bearing showed a through-ossification while of 9 less compressed joints only in 2 cases an ossified ankylosis of the joint was beginning or just in progress.

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DOES IMMOBILIZATION AND PRESSURE BEARING OF A JOINT RESULT IN OSSIFICATION IN AN ANIMAL EXPERIMENT?

K. Walcher and H. Stuerz[1]

Introduction

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The joint is an organ of movement, and movement is a prerequisite for the functional intactness of the joint. The degree of movement and direction, as well as the resultant action of mechanical forces, determine the form and structure of the joint on the large scale and the fine detail of the structural element on the small scale.

Immobilization and uniform, unilateral mechanical stress produce significant pathophysiological reactions in blood flow and metabolism.

The duration and nature of immobilization or abnormal stress are certainly of critical significance in determining whether a resultant limitation of function remains reversible or irreversible, and can therefore cause changes in a joint alone or in conjunction with other factors which, even after the cause is removed, cause the joint to be useless, to the extent of partial or complete fracture of the joint.

A resting position for joints is frequently unavoidable from the clinical and therapeutic standpoint. Numerous authors have dealt in their clinical and experimental studies with the consequences of this measure. Only a few authors believe that stable fixation even over a long period of time causes no permanent damage.

Kuentscher was able to show in the clinic and in animal experiments that a joint which has had a nail driven through it and been absolutely stabilized, remains surprisingly mobile even years after the nail has been pulled out. Kuentscher sees this as a confirmation of Boehler's view that an exact resting position for a joint need not necessarily lead to stiffening.

*Numbers in the margin indicate pagination in the foreign text.

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Most authors; however, assume that considerable damage is caused by immobilization (Chapchal; Cotta; Friedebold; Hall; Heiperts; König; Matthias and Glupe; Mohing; Rössler; Schneider; Watson-Jones; etc.). The damage found in the joint is particularly significant when pressure and friction, i.e., incomplete immobilization and pressure bearing, are also involved.

Previous Studies

Studies in animal experiments have shown that the morphology of the immobilization and compression injury to the cartilage of the joint and the subchondral bone shows agreement in certain respects to the degenerative changes in arthrosis deformans in man (Trias; Trueta; Trueta and Trias; Evans et al.).

Representations of metabolic dynamics in the damaged joint, obtained with the aid of autoradiography, have proven particularly useful in the interpretation of the degenerative changes (Thaxter et al.; Titze; Titze; Titze and Leb), as have quantitative biochemical analyses of various components of the ground substance of the cartilage (Ginsberg et al.; Curtiss and Klein).

To study the changes in the joint caused by immobilization with and without simultaneous compression by a mechanical device, a number of different animal experiments have been carried out recently (Figure 1):

1. Fixation of the knee joint of the rat in a middle position by cerclage between the femur and tibia (Hall, 1963).

2. Fixation of the knee joint of the rabbit in the extreme flexed position by hemicerclage between the femur and the tibia (Matthias and Glupe, 1966).

3. Fixation of the knee joint of the rat in the middle position by a plexiglass splint between the femur and the tibia (Evans et al., 1960; Thaxter et al., 1965).

4. External compression of the knee joint of the rabbit by means of a device similar to the clamp suggested by Charnley for knee compression arthrodesis, with simultaneous fixation in a plaster cast (Treueta, 1956; Trias, 1961; Trueta and Trias, 1961; Salter and Field, 1960). /218

5. The same, but using two steel nails driven through the femur and the tibia without immobilization in a plastic cast (Southwick and Crelin, 1961; Crelin and Southwick, 1964).

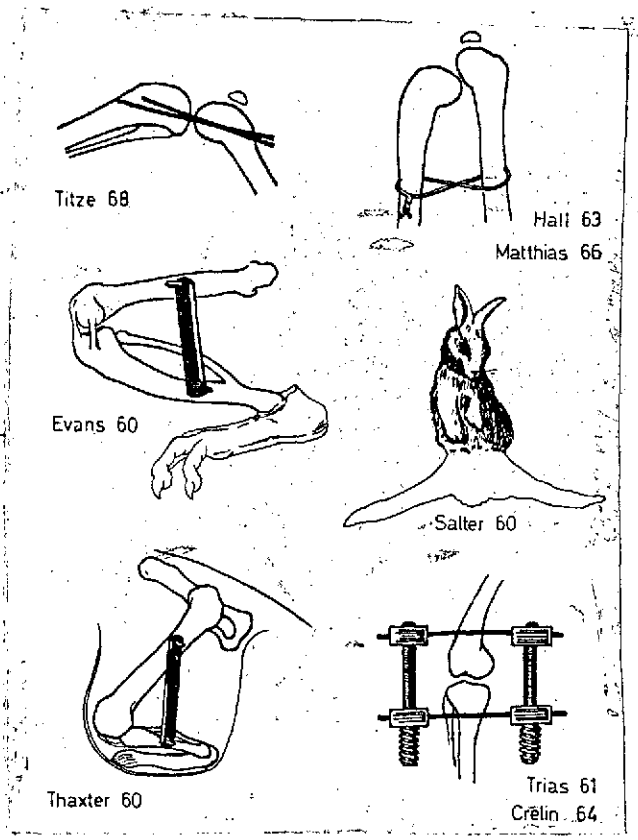


Figure 1. Illustration of the Experimental Procedure of Previous Researchers During the Last 10 Years.

6. Transarticular fixation of the knee joint of the rabbit with two Kirschner wires in a flexed position of 110-120° (Titze, 1968; Titze and Leb, 1968).

7. External compression of the knee joint of the rabbit with a Kirschner wire passed through the femur and the tibia; the wires are fastened by rubber bands (Ginsberg et al., 1969).

8. Fixation of the elbow joint in the rabbit with two extraarticularly located steel clamps, following previous intraarticular papain injections (Schneider, 1965).

9. Immobilization of various joints of the rabbit in extreme positions by plaster casts (Salter and Field, 1960).

In most of the experimental arrangements, the joint could be immobilized incompletely for only a short time.

An absolute resting position was achieved by Crelin and Southwick in one of their animals for 16 days, by Titze for about 3 weeks. Schneider was able to fix the joints completely until the bones fused.

Only estimates have thus far been provided concerning the compressive forces acting on the joint cartilage. Trueta and Trias estimated pressure levels of 21.0 to 28.0 kp/cm^2 in the bone contact area of compressed joint in the rabbit; Ginsberg et al., give compressive forces between 1.4 and 2.6 kp, without estimating the pressure.

The results of the research, in view of the altered experimental conditions, show considerable variation and are partially contradictory. Various fundamental observations, however, crop up repeatedly among different authors. Simple immobilization of a joint can cause prolonged damage, affecting primarily the joint cartilage. The creation of this damage is favored by the development of friction in the case of complete immobilization, and is further accelerated if additional pressure forces are active.

In addition to the general inactivity atrophy of the organ of movement, friction and pressure cause necrosis of the cartilage in the affected area, increased metabolism with an increase in cell count and cell size in the boundary areas, and characteristic changes in the quantitative composition of the ground substance of the cartilage.

In subchondral bones, conversion processes were observed which lead to the development of cysts. Atrophy and local hypertrophy of the subchondral trabecula are further products of the pressure-produced changes in the joint.

Statement of the Problem

The numerous abovementioned authors proceeded on the basis of quite different statements of the problem in their different experimental procedures, which were aimed primarily at the types of reactions in the cartilage, and less at the reaction of the subchondral bone to pressure and/or immobilization. The conditions in human arthrosis and particularly their etiology were to be studied together with the active compressive forces and their effects upon the joint.

We proceeded on the basis of the fact that the degeneration of the joint cartilage originates in lesions of the cartilage that result from improper pressure distribution over the joint area. Particular attention was devoted to the changes in the cartilage cells and the changes in the ground substance of the cartilage.

Titze studied the problem of damage to a joint caused by transarticular Kirschner wire fixation as the central point in his research.

Only Schneider carried out immobilization of the joint for the purpose of studying the fusion of the bone, ossal ankylosis. The ankylosis in the

experiments of Schneider actually occurred with absolute immobilization, but only after preliminary destruction of the cartilage by the proteolytic enzyme papain, which had to be injected several times intraarticularly.

Without destruction of the cartilage, as demonstrated by the above-mentioned experiment of Kuentscher, ossal ankylosis will not occur even after a long period of time, despite absolute immobilization.

Hence, a prerequisite for ossal fusion of a joint seems to be destruction of cartilage, combined with absolute immobilization.

Destruction of cartilage by injections of chemicals in the joint fissure was not successful. It was assumed that the mesenchymal tissue, which causes the bone to develop to cover the fissure in the joint, was destroyed by the injections.

According to Kuentscher, healing of pseudoarthrosis and occurrence of arthrodesis are familiar concepts. In both cases, it is elimination of a joint fissure that is involved, and it is not too important whether the fissure was created in the first case and inborn in the second.

A previous concept that synovial fluid hindered callus formation required /220
for reconstruction was disproved in animal experiments as far back as 1953 by Gelbke.

On the other hand, necrosis and disappearance of cartilage under the influence of pressure have already been demonstrated by numerous animal experiments.

We continue to encounter the question of whether the changes in the cartilage and bone mentioned by previous investigators can be modified by various degrees of compressive force.

It is also interesting to determine whether the time factor plays a role. In particular, however, it is necessary to try to clarify the question of whether absolute immobilization and certain amounts of pressure bearing without operative removal of the cartilage can cause ossal fusion of a previously healthy joint. What forces and what immobilization times are required for this?

In the animal experiments, as in the clinic, the main problem was and still is (in conjunction with studies of ossal fusion of a joint as well as in a fracture or pseudarthrosis) precise immobilization, which in arthrodesis (due to the long lever arm) poses technically much greater difficulties than in the case of a fracture or pseudoarthrosis at approximately the middle of the shaft.

Since none of these experimental arrangements appear to be suitable for the specific problem in question, a possibility of achieving a resting position was sought, in which:

1. complete immobilization could be ensured for long periods of time and
2. a certain degree of pressure bearing could be accomplished simultaneously.

Many tests have shown that in animal experiments complete immobilization for long periods of time without simultaneous use of monstrous plaster casts can be achieved only by combining internal fixation with the possibility of certain degrees of pressure bearing.

Will the pressure produced intraarticularly with the same experimental arrangement be capable of achieving in a mechanical fashion or by means of pressure-produced nutritive disturbances what Schneider was able to do by means of enzymes, i.e., the destruction of the hyaline cartilage, in order to cause ossal fusion?

Further considerations raise the question of where, in the case of ossal ankylosis, the fusion of the bone begins....at the center of the action of the pressure, or further toward the periphery? What types of ossification can be seen? Do the menisci create a form of barrier which possibly hinders the fusion of the joint or at least delays it?

From orthopedic surgery we know that joints kept in a resting position alone, as well as in a resting position with time-limited pressure bearing, even assuming preliminary damage to the cartilage, do not lead to fusion in most cases, and so it would appear to be an inflammatory event.

The cause of the lack of ossal fusion of the joint has been discussed: relief of the pressure bearing imposed in the operation, incomplete

immobilization, i.e., small movements in the arthrodetic fissure, effects of lever forces through the length of the extremities, particularly on the hips, the menisci acting as an interpositum in the knee joint, sclerosis, cyst formation and necrosis in the subchondral space.

In our own animal experiments we attempted to determine the effect of precise immobilization combined with pressure bearing, eliminating the above-mentioned disturbing factors.

Materials and Methods

Preliminary tests showed that the knee joint of the rabbit was best suited /221 for the tests we planned. It is easily accessible and corresponds in size to approximately the middle joint of the index finger in man. Therefore, from the technical standpoint, it allows a difficult joint operation to be carried out.

Pressure Bolt Transfixing of the Joint

Immobilization and compression of the joint took place with a highly polished pressure bolt which we made out of V_4A steel, introduced in a right angle flexed position under sterile precautions from the head of the tibia transarticularly in the sagittal plane (Figures 2 and 3).

Figure 2. Pressure Bolt Made of V_4A Steel With Cutting Cap, Nut Calibrated Compression Spring.

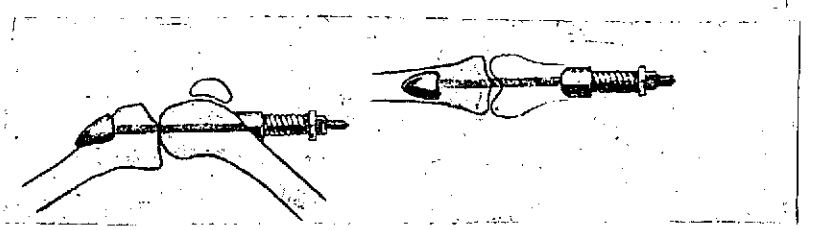


Figure 3. Transarticular Position of the Pressure Bolt, Which Was Passed in a Spacific Position Through the Fossa Intercondylica and the Intercondyl Massif and Thus Did Not Traumatize the Cartilage Contact Areas.

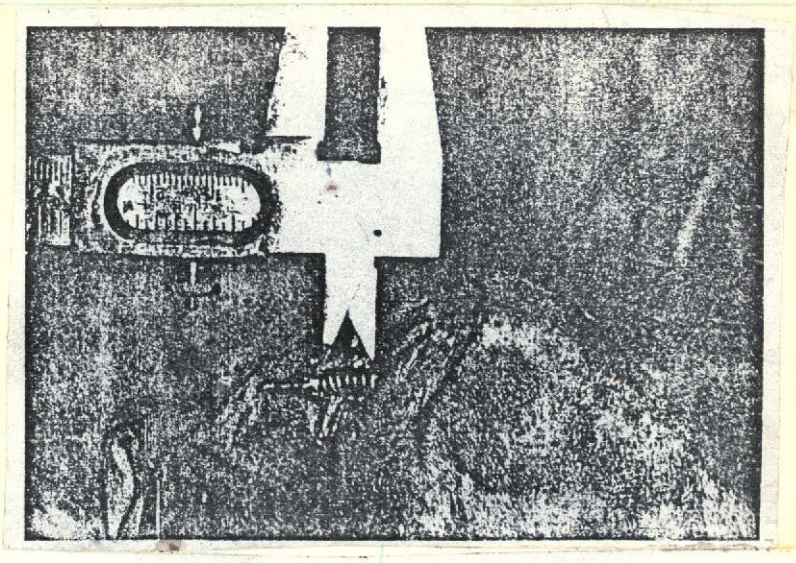


Figure 4. Desired Spring Compression Checked With the Aid of a Sliding Caliper.

The path of the bolt through the eminentia intercondylica of the head of /222
the tibia and the intercondylic fossa of the femur excluded tramatization of the joint cartilage by operative intervention. At the point where the bolt emerged on the distal femur, on the tensioned side directly proximal to the joint capsule duplication, a cutting cap suited to the anatomical conditions served as a counterbearing for a calibrated compression spring with a 4-sided nut that could be used to compress it to give the desired force. The length of the spring served as a measure of the force exerted.

The bolt was imbedded in the musculature of the femur and depressed beneath the skin, after which the shin of the operated leg was amputated at the distal third. Preliminary tests had shown that rabbits kept in individual cages rested their full weight on the immobilized leg immediately after awakening from anaesthesia. Forced rotary movements of the animals led to fractures at the point of emergence of the bolt on the distal femur. By reducing the play, the force causing the fracture were eliminated, and the force convalescence of the extremity eliminated the effects of additional intermittent compressive forces.

The use of this pressure bolt allowed absolute fixation of the joint for any period desired, with simultaneous application of a known compressive force (Figure 4).

Four to eight days prior to being sacrificed, the animals received 50 mg. of oxytetracycline (Terravenoes Pfizer) per kg i.v. Six hours before sacrifice, two mg per kg of S^{35} was given i.v. in an isotonic solution.

Division of Experimental Animals Into Groups

A total of 151 adult animals were used for the experiment. 81 of these could be evaluated exactly.

The compressive forces were set between 4000 and 24,000 p with 2,000 p differences in each case. Five to seven animals received the same degree of spring compression. One animal from each group was killed after 14 days, 1, 2, 3 and 6 months; both knee joints were immediately prepared and processed histologically.

The control groups were composed of animals whose knee joints were immobilized without compression, and animals which had only the right shin amputated.

For final evaluation, the animals with low, medium and high spring forces were summarized and compared with a fourth group of control animals.

Methods of Evaluation

The spring compression of the joints was effected intraoperatively by means of a sliding caliper and documented immediately postoperatively by means of an x-ray with a scale superimposed on it (Figure 5).

Continuous x-ray checks with a scale superimposed at 14-day intervals were used to check the selected position of the joint from 90 to 100°.

In the joint preparations, the following macroscopic individual criteria were checked after the compression bolt was removed: residual mobility quality and amount of synovial fluid, pannus formation.

From those joints which showed residual mobility, the femur and tibia were prepared separately and the condition of the menisci and the deformation of the joint elements were described and documented by photographs. The depth and extent of the so-called pressure zones on the cartilage contact areas were

described, and the areal dimensions of the cartilaginous lesions affected by pressure were determined, using a loupe with a millimeter scale on it. If ankylosis of the joint was found after the compression bolt was removed, x-ray photos were taken in two planes, and especially fine-focus pictures.

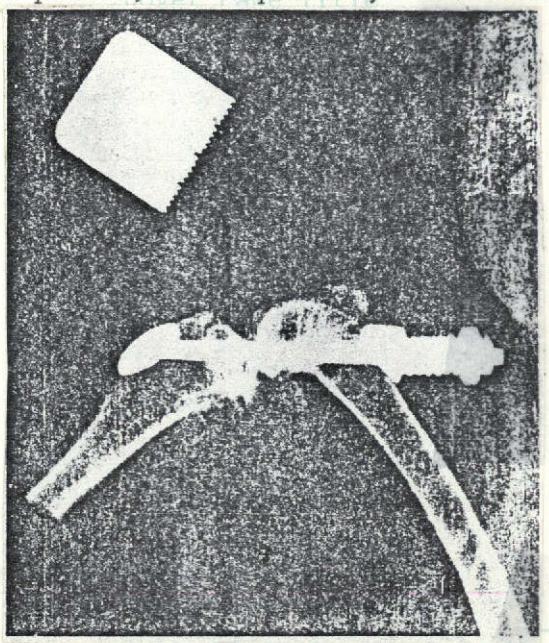


Figure 5. X-ray Picture, Later to the End of the Intervention With Simultaneously Superimposed Scale to Check Spring Compression.

The following was the procedure used in the histological technical preparation of the material:

The femoral condyles and the head of the tibia of the joints that were not ossally fussed were broken up into four individual pieces. The fibular or tibial portions of the condyles were fixed in Susa mixture and simultaneously carefully decalcified. The internal portion of the tibial condyle of the femur and the tibia was selectively stained according to Frose in basic fuchsin; the rate of development of the bone in thin bone sections was determined by means of photometry after tetracyclin had been given beforehand. This has been described elsewhere (Z. Orhop.).

The internal portion of the fibular condyle was fixed in Schaffer solution and then imbedded in methylmethacrylate. The method modified by Burkhardt, going back to Boellaard and von Hirsch, was used.

Paraffin blocks were made from the preparations fixed in Susa, and sections 5 microns thick were cut from them with the following stains: hematoxylin-eosin, Azan van Gieson and Goldner; in addition, the histochemical reactions to astra, alcian and toluidine blue were prepared. The alcian blue stain was combined with the PAS method according to Hotchkiss-McManus. The astro bule stain was counterstained with nuclear true red.

Two sections from each group were used for autoradiography. The "stripping film techniques" was used (Kodak film AR 10).

S^{35}, because of its half life of nearly 3 months, offers a broad range of exposure latitude; however, the optimum exposure was determined in preliminary tests and found to be 17 days. Development was followed by staining with hemalum, since staining with hematoxylin-eosin proved less suitable.

Microtome sections three microns thick were cut from the preparations imbedded in the plastic and subjected to the following stains: Giemsa, Ladewig. In the case of special problems under study, the PAS method and silvering according to Gomori were used.

Joints which proved to be fused (on the basis of mechanical tests and x-ray pictures) were cut in half by a sagittal medial cut and each half was imbedded in paraffin or acrylate. The blocks obtained in this fashion were prepared completely in series sections and subjected to periodically repeated stainings: hematoxylin-eosin, azan, van Gieson, PAS-alcian blue, astra blue, nuclear true red, toluidine blue. The abovementioned stains were prepared from the acrylate sections. /224

Preparations were likewise obtained from the left knee joint of each animal using the same method and utilized in microscopic evaluation as individual controls for the operated joints.

Results of the Study

With respect to the principal problem under discussion here, we can assume the following in advance regarding the experimental procedure described: Under certain conditions, there is ossal joint fusion. A number of additional individual observations were made. Macroscopically and microscopically, the

effects of pressure upon the joint lead to extensive modifications of the joint components, causing restructuring of the joint.

First we shall describe only the mechanical effects, showing the numerous forms that the changes in the joint can take, and then the ossal restructuring of the joint will be discussed.

Immobilization and Compression During the Experiment

The measurement of the spring force with the sliding coliper at the beginning and end of the experiment, as well as the checks performed with the x-ray pictures during the test, show the same regular percentile decrease in force with time in all animals, regardless of the original spring force. The average decrease in force in all animals after 14 days was 25%, after 1 month 50%; from then on the spring force remained unchanged for the rest of the experiment (Figure 6).

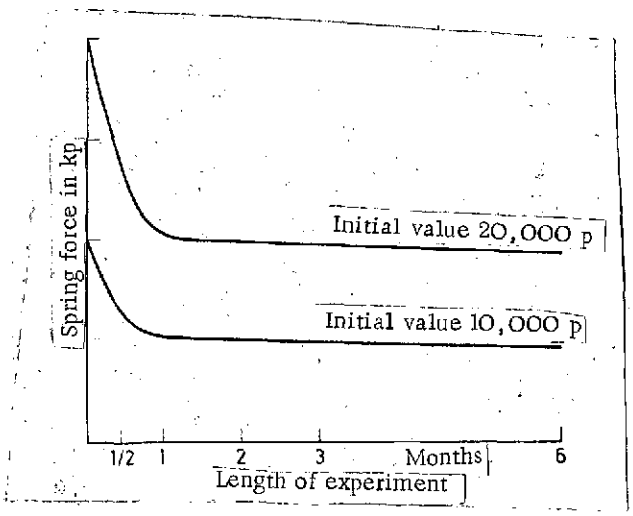


Figure 6. Decrease in Force of the Calibrated Compression Springs in the Course of the Experiment.

In order to calculate the actual pressure values in the cartilage contact area, a size determination of the cartilage contact zones is necessary. This is only possible at the end of the experiment during preparation, and examination by means of a loupe will show only the final state. The pressure zone was assumed to be an area which, in contrast to the environment, showed clearly visible changes such as flattening, edge formation, loss of sheen, changes in color and consistency of the cartilage, or complete loss of cartilage.

The size and shape of the pressure marks varied between circular (with a diameter of 3 mm) and nearly square (4 mm on a side) but a clear definition of the extent of the pressure zone was not always possible. /225

Contact areas between 14 and 32 mm^2 were calculated, corresponding to 1/7 to 1/3 cm^2. When using high spring forces and long time intervals, pressure

marks were larger and deeper as a rule than for low spring forces and brief intervals.

When the approximate values obtained were used, pressure levels were recorded in the cartilage contact area which reached up to 120 kp/cm^2 in Group III, and up to 90 to 50 km/cm^2 in Group II and Group I.

Macroscopic Findings

Depending on the period of immobilization, and initially independently of the applied pressure, after the pressure bolts were removed the joints showed an increasing limitation of mobility.

Following immobilization times of 14 days to 4 weeks, there was still a residual mobility of approximately 30-50°, after which residual mobilities of 10 to 20° could be seen. Following an immobilization time of 3 months or more, a fibrous stiffness developed, which allowed only slight oscillating movements. After overcoming of the hard bearing surfaces with forced bending and stretching, the superficially modified capsule and the shortened tendons and strips tore, with a definite cracking sound. Following an immobilization period of 6 months, and especially when using higher pressures, complete stiffness of the joint was observed, which in preparations proved to be fibrous in a small number of cases and ossal joint ankyloses in a large number of cases.

If the resting position was maintained, the joints dried out completely. /226
Beginning with the 4th week, the cavum of the joint was increasingly filled by initially tough, later hard adhesions and finally extensive joint pannus. The pannus connective tissue could only be separated more sharply from the joint elements after six months.

The joint cartilage lost its sheen and transparency in the pressure zones. The cartilage was dull grey to brownish-yellow; when touched with forceps, it showed an increasing degree of softening. The higher the pressure and the longer the resting position, the larger were the pressure marks as a rule. In particular, the femur condyles were deformed to an increasing extent, while the head of the tibia showed hardly any change in shape (Figures 7 a and b).

The menisci became narrow, thin, flaccid, glassy and transparent as the length of the experiment increased; a tough fibrous ring was retained only at the external circumference. After 6 months, the remaining miniscus could be completely separated from the pannus only following sharp preparation. It was also studied histologically and histochemically. The immobilization and pressure-produced changes are described elsewhere.

When dividing the preparations with a very fine fret saw, the slightly harder consistency of the unoperated joints could be clearly seen in contrast to the operated joints. In the case of the compressed joints, it was only during separation of the subchondral bone in the pressure zone that increased resistance was felt momentarily.

Microscopic Findings

Degeneration and Necrosis of Cartilage in the Pressure Zone Area:

In 1960, Salter and Field proposed a division of pressure-produced joint modifications into stages which established 3 degrees of macroscopic and microscopic indications. This division, which begins with loss of nuclear staining and ends with a complete loss of cartilage, has been adopted by almost all later authors and has proven suitable in our observations as well:

First Degree

Macroscopy: loss of sheen and transparency of cartilage, yellowish-white color, perceptible softening.

Microscopy: no stainability of the nuclei of the chondrocytes in the surface and transitional zones, various patterns of nuclear changes in the deeper cartilage layers.

Second Degree /227

Macroscopy: partial loss of thickness of cartilage at the center of the lesion, changes at the edges according to the first degree.

Microscopy: complete disappearance of surface and transitional zones of cartilage, loss of stainability of cells and ground substance in all other layers. Scattered hypertrophy of the subchondral bone.

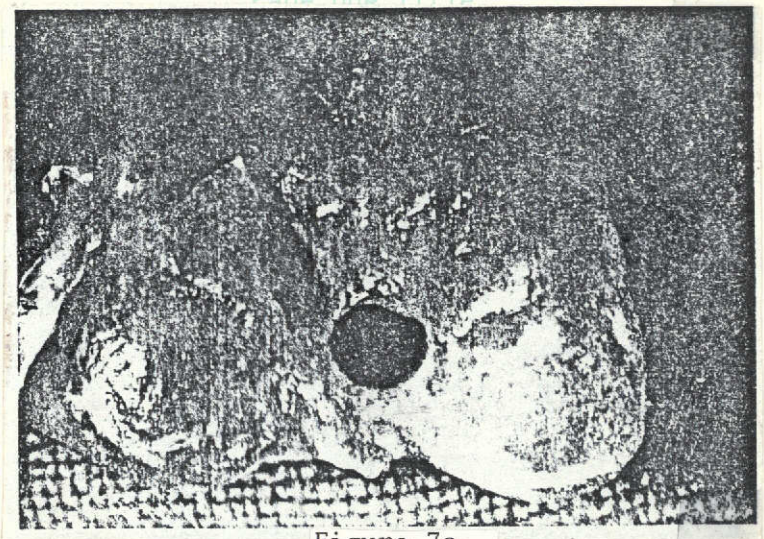


Figure 7a.

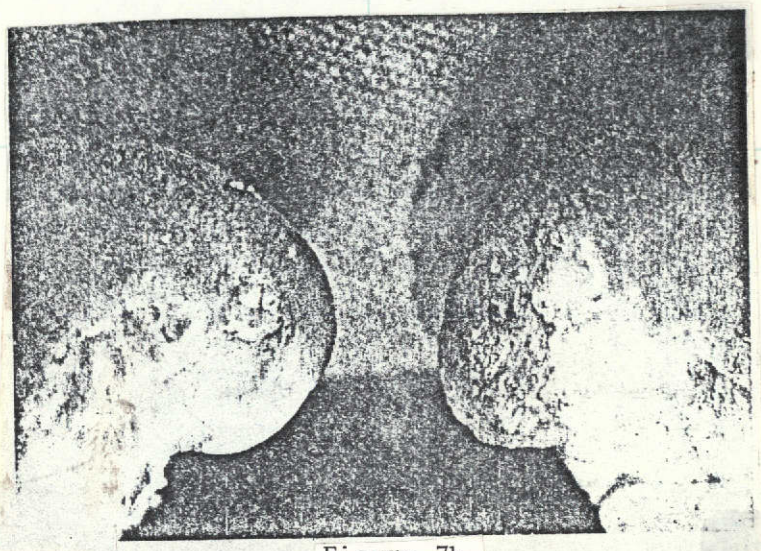


Figure 7b.

Figure 7. (a) Definite Pressure Marks Above the Femur Condyle Following 3 Months of Immobilization and Subjection to Pressure. The Bolt Canal Can Be Seen in the Area of the Fossa Intercondylica; the Cartilage Contact Areas Have Not Been Damaged By the Bolt Canal. (b) Deformation and Flattening of a Femur Condyle Following 3 Months of Immobilization and Subjection to Pressure, With the Left Condyle of the Femur Shown for Comparison.

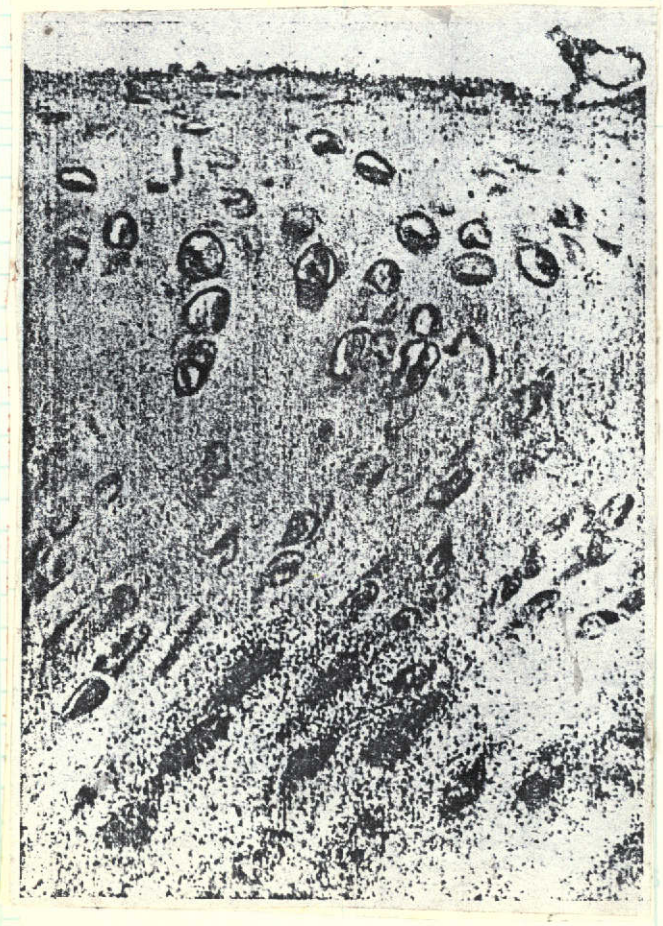
Third Degree

Macroscopy: disappearance of cartilage throughout entire thickness; the subchondral bone is free in the middle of the lesion.

Mircoscopy: complete disappearance of chondrocytes and intercellular substance in the center of the lesion, with changes of the second and third degree toward the periphery. Definite hypertrophy of the subchondral bone.

The changes show the same pattern in our own material.

Histochemical reactions also show that before visible changes occur in the cartilage cells or their nuclei, the first pressure-produced changes cause disappearance of the basophilia and metachromasia of the cartilage territories, /228 i.e., loss of stainability with alcian, astra and toluidine blue.



To the extent that they are retained, the cells or cell remains at the center and at the edge of the pressure lesions lose their radial arrangement. The rows of cells extend laterally toward the edge of the pressure zone. There the cells are large and vesicular, showing diverse cell tears and various, mostly intensified nuclear stainability. The cells and the surrounding ground substance are increasingly stainable with basic dyes, but this feature disappears with increasing distance from the pressure zone.

Figure 8. Clear Labelling of the Lower Cell Layers at the Center of a Pressure Zone After Administration of Radioactive Sulfate, 8 Hours Prior to Sacrifice. Cells of the Superficial Layers and the Radial Layer Still Colored, But No or Very Little Labelling (Paraffin, Stripping Film Technique, Hemalum), 800X.

Nuclear stainability in the area of a pressure zone does not mean retention of metabolic activity. This can be demonstrated autoradiographically following labelling with radioactive sulfate. While the lower layers at the center of a pressure zone display a clear labelling, the upper layers can still be distinguished by their color but they show no sulfate inclusion (Figure 8).

Finally, at higher pressure values, it is no longer possible to see extensive deposition of cartilage reticulated bone finally appears at the center of the pressure zone, in which hyaline cell and ground substance areas occur to an increasing degree.

Changes in the Cartilage

Simultaneously with the destruction of the cartilage at the surface, there is a continuing ossal replacement of the joint cartilage, proceeding outward from the marrow space. The ossification process, which normally takes place in the basal cartilage layers, now appears to proceed at an accelerated pace. Partially large-caliber vessels spread out from the marrow into the cartilage, bordered by ossal ground substance producing osteoblasts. (Figures 9 a and b). The ossal substance, growing forward with an irregular front, continues to display cartilage cells and cell remains as well as ground substance, stained to different degrees. Various cartilage areas surrounded on all sides by bone temporarily display increased basophlia of the plentiful ground substance; the enclosed cells are swollen and accumulate in piles. Finally, these /229 islands of cartilage in the newly formed reticulated bone show continuously decreasing amounts of remains of cartilage cells or ground substance.

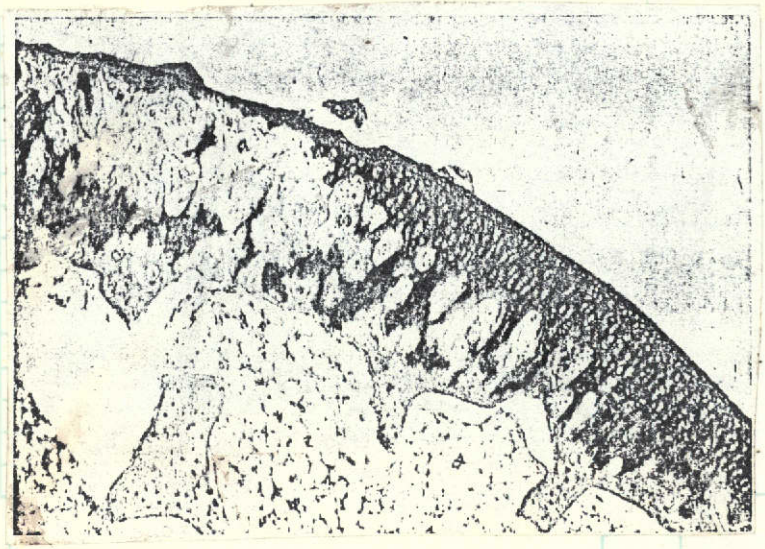


Figure 9 a.

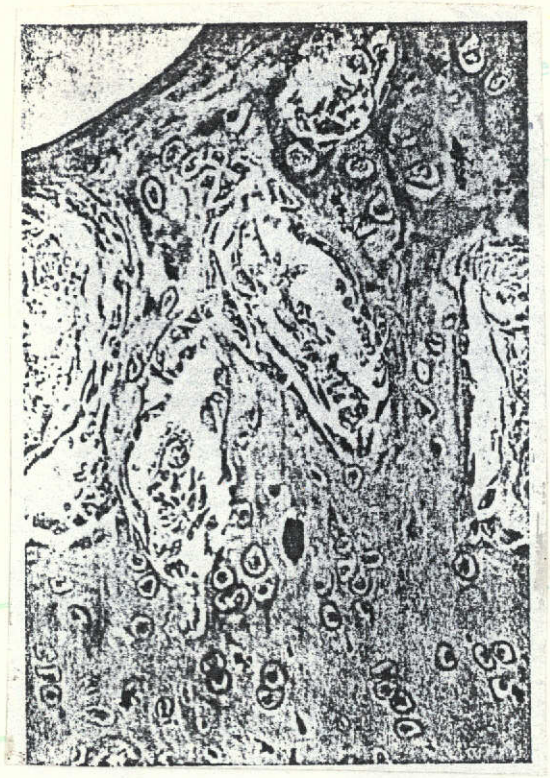


Figure 9 b.

Figure 9 a. Edge of a Pressure Zone: Growth of Large Caliber Vessels With Numerous Endothelial Cells and Osteoblasts. Extensive Bony Replacement of the Joint Cartilage. Remainder of Astra Blue Positive Cells and Cartilage Ground Substance in the Newly Formed Bone Ground Substance (Paraffin, Astra Blue, Nuclear True Red), 375X. b. Cartilage Largely Reconstructed to Form Bone. Remainder Usually Only More PAS--Positive Ground Substance, Corresponding to the Former Calcified Zone, in Newly Formed Bone (Paraffin, Alcian-PAS), 150X.

Atypical Chondrones

Atypical chondrones have been described on many occasions by previous investigators; they are composed of accumulations of chondrocytes with highly basophilic capsules, and therefore are quite similar to the previously described nests of cartilage cells (Figure 10). Most investigators see reactive cartilage cell activations in them, constituting an insufficient attempt at regeneration. This is indicated by the histochemically and autoradiographically demonstrated increased metabolism of these structures. We found them not only at the edge and base of cartilage pressure zones, but also everywhere that the described reconstruction of the cartilage took place, particularly in the vicinity of the infiltrating capillaries. Atypical chondrones could be found in the joint cartilage of joints that were merely immobilized and not subjected to pressure.

Pannus Formation

After one and up to two months, one could see connected tissue tongues spreading into the joint fissure, extending from the edge of the joint cartilage (Figure 11). Up to this point in time, the connective tissue could still be separated from the joint cartilage. Later, the pannus and fibrously modified superficial cartilage layers become continuously merged with one

another, so that after 6 months no definite conclusions could any longer be drawn regarding the origin of the thick connective tissue which fills the entire joint fissure.

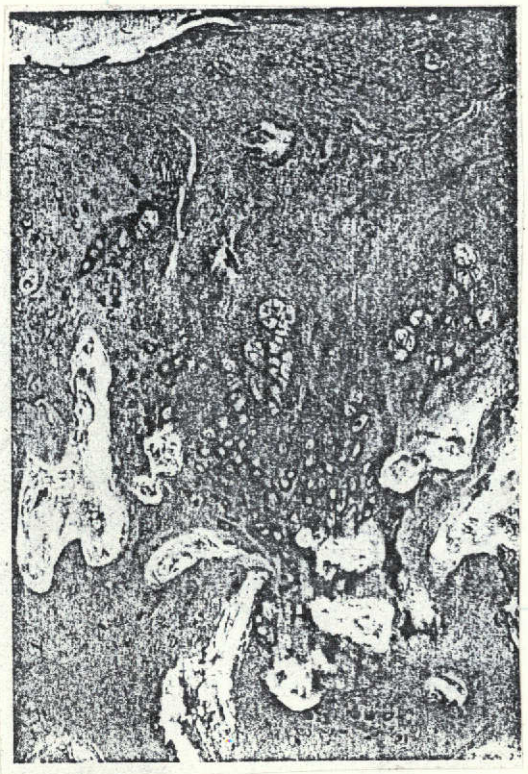


Figure 10. Cartilage Cell and Cartilage Ground Substance Remainder in the Depths of the Subchondral Spongiosa. Partially Large Caliber, Newly Formed Vessels From the Narrow Space, Spreading in the Direction of the Surface of the Joint. Large Vesicular Cartilage Cells Occur Separately or Arranged Into Atypical Chondrones. Alcian Blue Positive Ground Substance Occurs Only in the Immediate Vicinity of the Cartilage Cells and Atypical Chondrones (Paraffin, Alcian-PAS) 150X.

Fibrous Cartilage

Fibrous cartilage as an expression of reparative processes appeared only after two months, but then could be found regularly. The ratio of cells to fibres was highly variable, and often there was a clear transition in the fibres-rich joint pannus. A transition from fibrous cartilage to retained hyaline joint cartilage could not be seen, but there probably was a continuous connection of fibrous cartilage to the formerly subchondral bone.

Behavior of Subchondral Spongiosa

The joints that were immobilized without compression all showed atrophy of the trabecula and rarefaction of the subchondral spongiosa; in the compressed joints, the situation was somewhat different. Here, directly beneath the cartilage contact point, there was hypertrophy of the trabecula with narrowing of the mesh, and finally a strip of compact bone developed. Outside the pressure zone, however, there was more travecular atrophy, so that we could only speak of local hyperostosis.

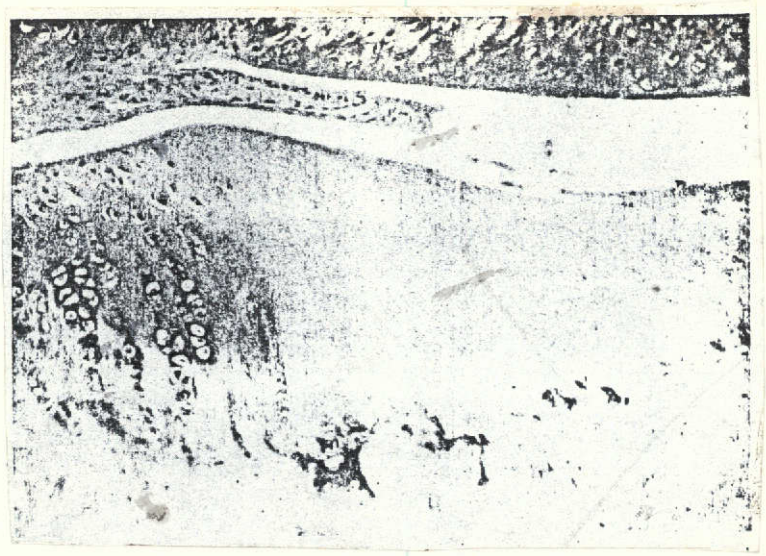


Figure 11. Tongue-like Growth of Cell-rich and Fibre-poor Adhesions Between the Opposite Joint Surfaces. Second Stage of Cartilage Degeneration, With Large Vesicular Cartilage Cells at the Edges of the Pressure Zone (Paraffin, Astra Blue, Nuclear True Red), 375X.

Ossal Fusion of the Joint

Following long periods of immobilization and use of mostly higher spring forces, some of the animals developed incipient to far advanced ossal fusion of the joint. In Group I, (spring force 4 to 10 kp) one animal out of five showed ossal ankylosis; in Group II (spring force 12 to 16 kp), there was one case of ossal fusion in four animals, and in Group III (spring force 18 to 24 kp) five out of six animals showed ossal fusion of the joint fissure. There was no ossal fusion in the various control groups.

In the preparations, completely arrested mobility was restored in these joints following removal of the pressure bolt; X-ray pictures in two planes, as well as special fine-focus pictures, in comparison with the opposite non-operated side, showed complete disappearance of the joint fissure, distortion or deformation of the condyles of the femur, and finally increased sclerotization in the former area of the joint fissure, with fused structures observed occasionally (Figures 12 a and b).

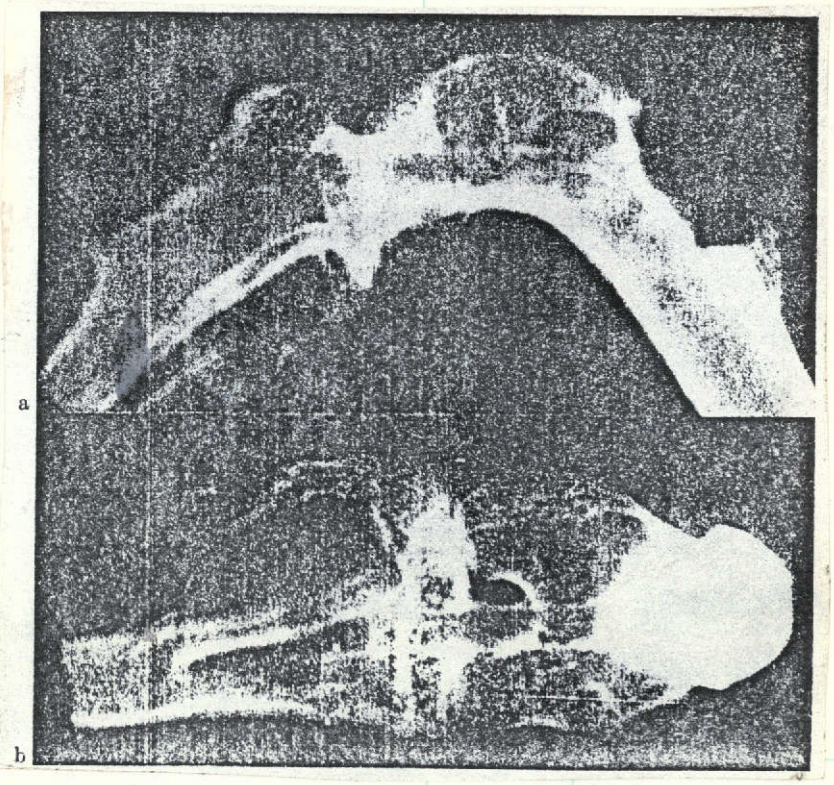


Figure 12 a and b. Fine-focus Pictures of a Prepared Knee Joint Following Six Months' Immobilization and High Pressure. Pressure Bolts Already Removed. Joint Fissure No Longer Visible; Through Bony Structures, Increased Sclerosis.

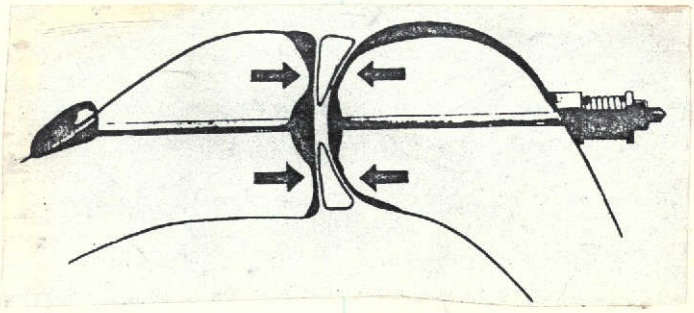


Figure 13. Beginning and Continuation of Ossal Fused Structures, Not in the Center of the Contact Areas and Pressure Zones, But at Their Edges, at the Level of the Menisci.

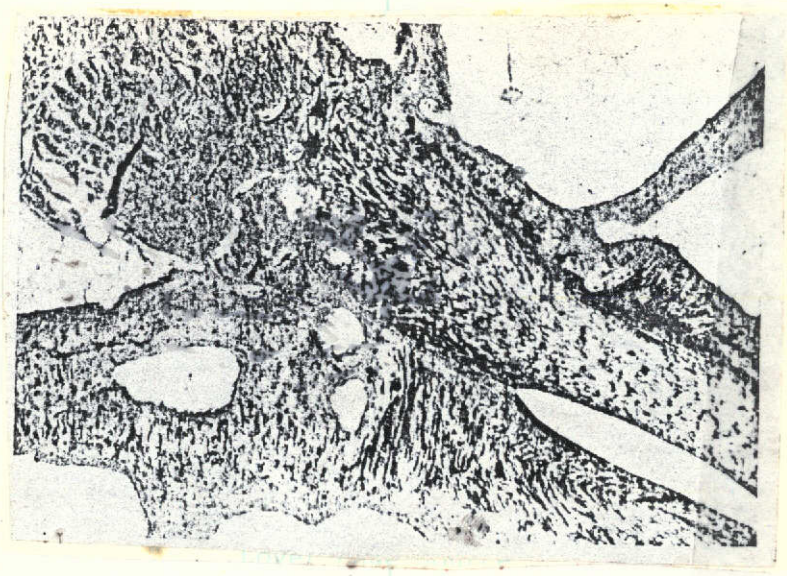


Figure 14. Incipient Ossal Fusion (Center of the Picture and Top Left) At the Level of the Meniscus (Center of the Picture and Right). Nodular Accumulation of Cartilage Cells of Meniscus Tissue, Strongly Stained With Basic Dyes, With Approach to the Areas of Ossification (Paraffin, Astra Blue Nuclear True Red), 50X.

The series sections of the stiffened joints showed, surprisingly, that the ossification process does not occur as anticipated at the center of the pressure marks in the area of pronaunced cartilage pressure necrosis. Instead, as a rule, at the level of the menisci, partially at the base of the meniscus, but still more frequently at the level of the central part and extending out to the point, two bony barriers developed which bridged the joint to an increasing degree, serving as the source for further ossal fusion of the joint (Figure 13). The ossal fusion began at the edges of the pressure zone, in other words, at the point where only cartilage pressure necrosis of Grades I to II according to Salter and Field had developed.

Possibly the pressure, which initially had its effects only at the center /233 of the joint, was displaced toward the periphery, and later disappeared or largely vanished at the center as an expression of pressure necrosis on the cartilage. The reconstruction of the cartilage which has been described, with the spreading of osteoblast-filled vessels outward from the subchondral space, continued out through the meniscus tissue, with the cells of the menisci

basically behaving like the chondrocytes of the joint cartilage. The ossification processes in the femur and the tibia merged, so that finally there was a combination of the bony parts in the meniscus tissue (Figure 14).

The fact of the incipient ossal fusion at the level of the menisci could be shown particularly clearly in survey pictures of the reconstructed joint. There was a similar observation: the central joint fissure was free and still retained, and there was a narrowing of the corresponding cartilage contact areas, associated with more or less pronounced pressure necrosis. At the level of the menisci there were ossal barriers, which had already caused a merger of the joint chondyles. The actual meniscus tissue occurred only in residual amounts, usually in the form of meniscus points, in the immediate vicinity of the newly formed bone (Figure 15). Therefore, themenisci did not display the characteristics of an interpositum which hindered ossification, but instead took a vigorous part in the ossification process.

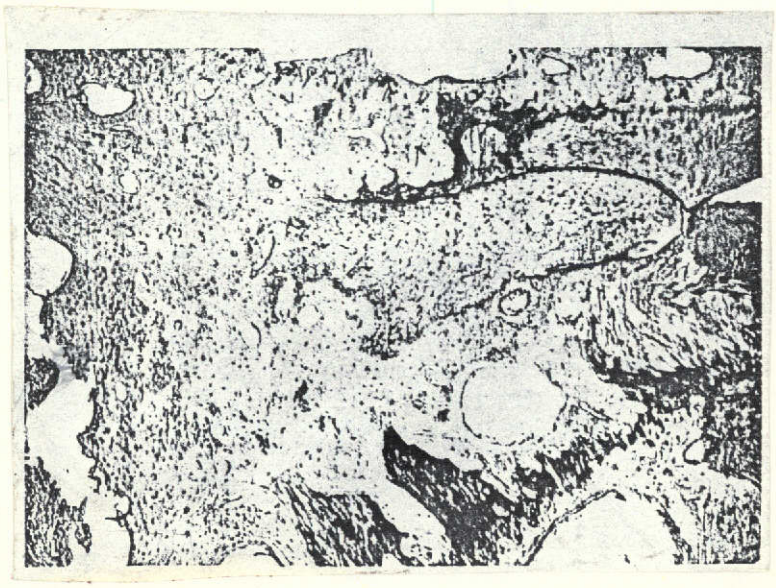


Figure 15. Increasing Ossal Replacement of the Meniscus Whose Tip (Center of the Picture and Right) Is Walled in on All Sides By Bone (Paraffin, Alcian-PAS), 50X.

In the course of this ossal reconstruction, particularly within the hyaline cartilage, histological pictures develop which are reminiscent of the mode of chondral ossification. The reconstruction of the cartilage always begins in the subchondral space, with the initial appearance of small and large caliber vessels. As the vascular connective tissue approaches and neoformation of the bone begins, the cartilage cells enlarge, swell and become large vascular cell elements. They produce ground substance in increased amounts, and the cartilage capsules themselves show increased basophilia (Figure 16).

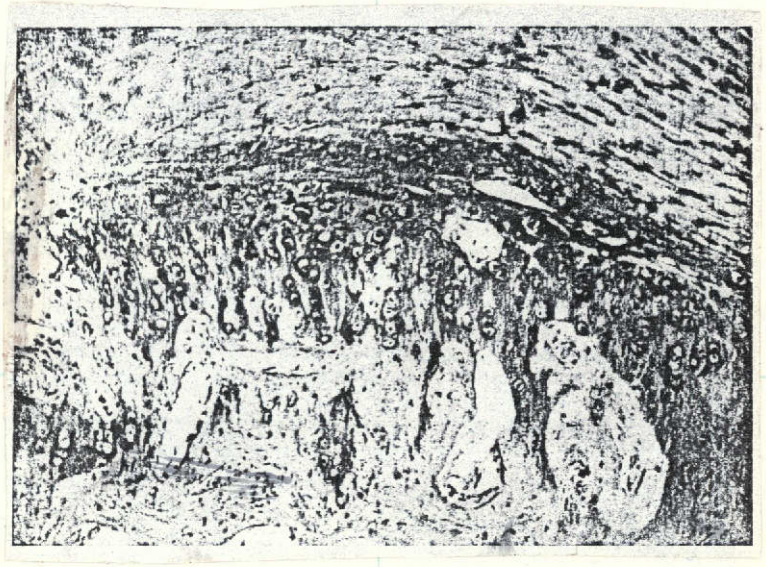


Figure 16. Increasing Reconstruction of Cartilage Following Spreading of Numerous Vessels From the Subchondral Area. Bone Formation Around the Vessels. Swelling and Increased Stainability of the Cartilage Cells, With Incipient Cartilage Degeneration at Other Points. In the Area of the Border of the Meniscus, There is an Increased Amount of Ground Substance That Can be Stained (Paraffin, Astra Blue, Nuclear Ture Red), 125X.

The simultaneous development of the newly formed bone substance around /234
the vessels partially extends in the from of islands or strips into the various cartilage areas; on the other side, in the area of the front-like cartilage bone boundary areas, there are extensive lacuniform recesses in the cartilage ground substance (Figure 17).

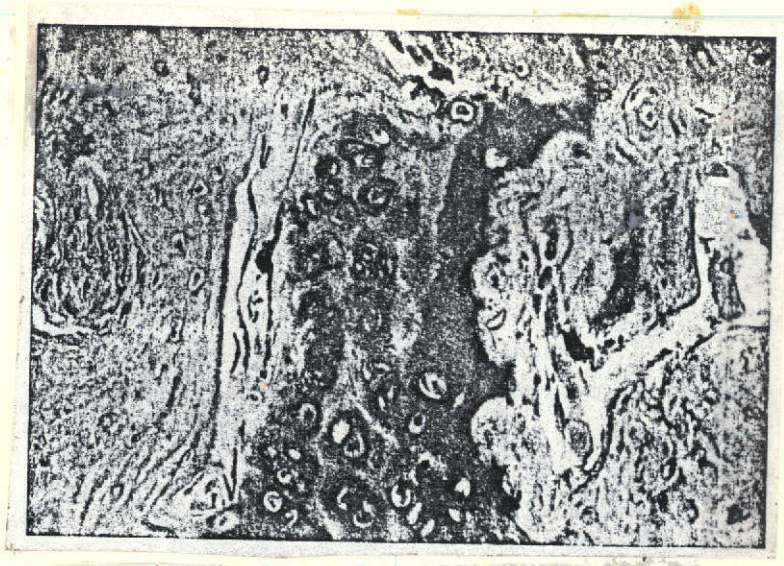


Figure 17. Lacuniform Breakdown of the Highly Basophilic Cartilage Ground Substance in the Vicinity of the Newly Formed Vessels. Extensive Ostioblast Margins at the Left of the Picture.

A number of the chondrocytes appear changed into chondroclasts in these stages. This is indicated by the halo free of ground substance which appears abound the cells, which now act as cartilage destroyers (Figure 18). As the process continues, the initially richly produced ground substance, decimated on /235
several sides, shrinks until only circular and finally cap-like remains exist around the chondroclasts (Figure 19). The cells which act as the destroyers of the cartilage show a change in their cell contours and the formerly smooth surfaces of the cartilage cells become irregular and partially spinose. Finally, after extensive chondroclasia, the pronounced basophilia of individual cartilage capsules resembles the cartilage ground substance in color only.

Whether the osteoblasts and osteocytes which now appear come from the mesenchymal and endothial cells which accompany the vessels, and whether these cells therefore originate from indifferent cells, which occasionally produce cartilage and occasionally bone, or whether this is a further development of chondrocyte- /236
-chondroclast-osteoblast-osteocyte or chondrocyte-osteoblast, seems to vary from one individual observation to the next.

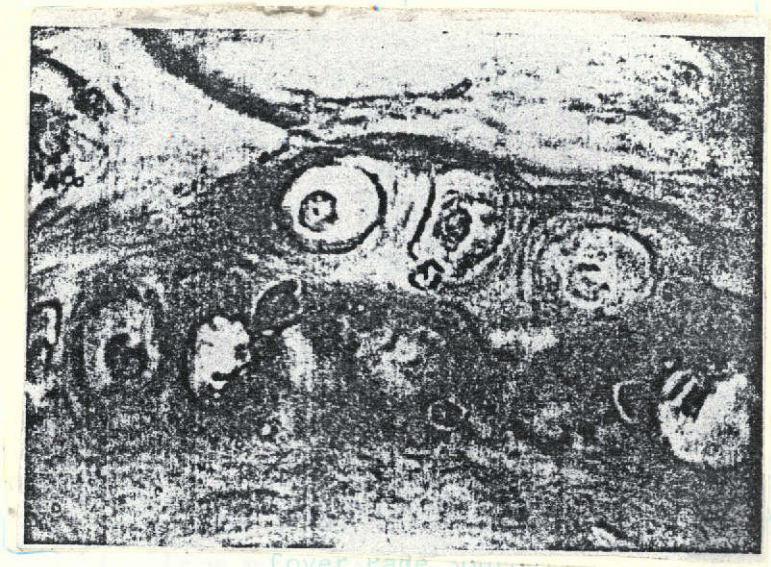


Figure 18. Conversion of Chondrocytes Into Chondroclasts Which Come to Rest in a Halo Free of Ground Substance (Paraffin, Astra Blue - Nuclear Tone Red) 1250X.

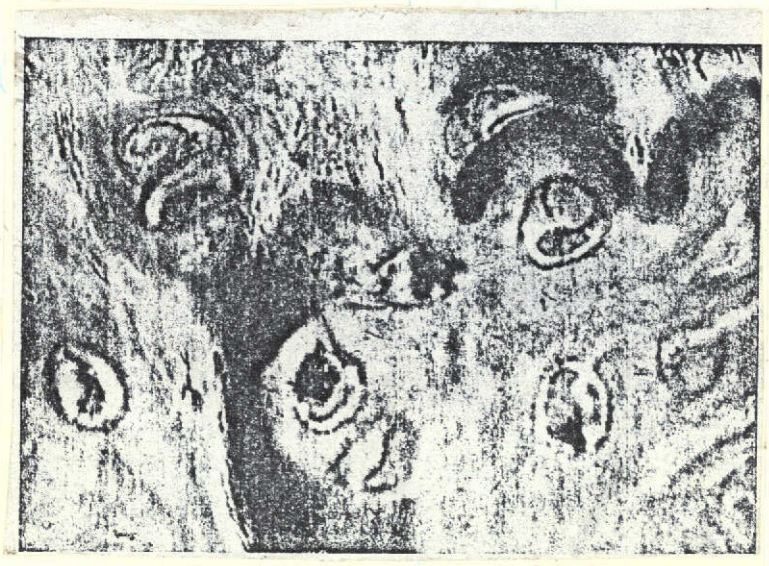


Figure 19. Disappearance of Cartilage Ground Substance to Semicircular or Cap-Shaped Remainder (Paraffin, Astra Blue, Nuclear Tone Red) 1250X.

There is one constantly recurring observation that is striking, however; cell elements that undergo the change described above occur in newly formed bone tissue which is surrounded by recesses of reamining cartilage ground substance (Figure 20).

On the other hand, a portion of the chondrocytes which initially produce large amounts of ground substance (and are therefore metabolically active) are destroyed, with other cell elements taking part in the destruction of the cartilage ground substance, finally "dying out" in the cartilage ground substance that forms in the meantime. Under the optical microscope, it is impossible to find any satisfactory answers as to the significance of these cell changes; Knese and Knob stress this in particular.

Finally, during and after the stage of chondroclasis, various cells appear to an increasing degree, whose surface show spinose extensions to an increasing degree which are reminiscent of the protoplasmic extensions of the osteocytes. The circular shapes of the chondrocytes are also lost and the cells become more rounded or flattened.

Finally, in the ossal fusions which develop from one condyle to the next there are scattered cartilage cell remains and residue from the corroded cartilage ground substance in strip-form, later lattice-like, parts which are completely irregularly scattered. These remaining cartilage ground substance areas are mostly only more PAS-positive; occasionally in their centers there are red or pink cartilage ground substance areas, which show up only under alcian blue (Figure 21). These cartilage cell and cartilage ground substance remains also demonstrate the phenomenon of metachromasia, with the individual cartilage cells that are still retained showing a halo of ground substance with increased metachromasia (Figure 22).

These images are also reminiscent of stages of further advanced menchondral ossification of the growth fissure. Within the perichondral ossal sleeve, there are enchondral ossal travecular, which enclose the remaining calcified ground substance.

This mode of ossification, in which the hyaline cartilage and remaining meniscus assume a place-holding function for the new bone, provided a predominant

amount of the bone neoformation which is observed, but there are also other possibilities of ossification that were observed, although to a much lesser degree. In studying the series sections of other joints, a type of ossification was found which differs from the one seen so far.

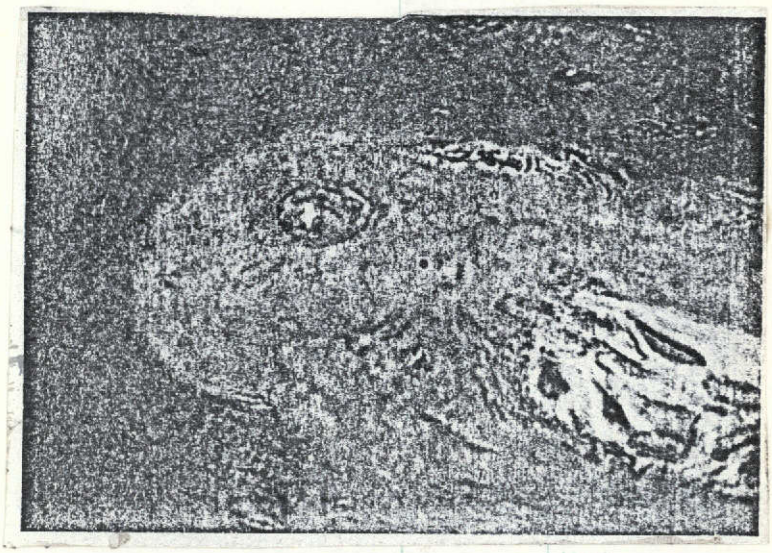


Figure 20. Individual Osteoblast in Newly Formed Bone Ground Substance (Paraffin, Astra Blue, Nuclear True Red), 1250X.

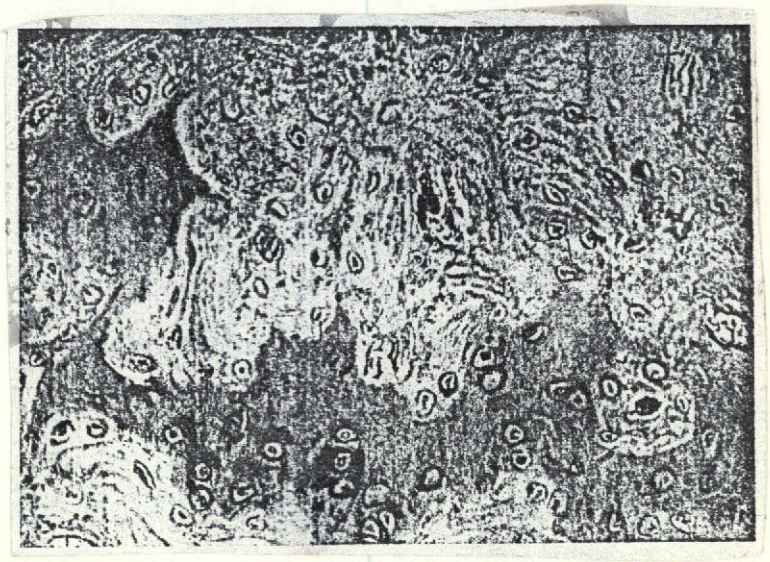


Figure 21. Strip to Lattice-form Cartilage Remains, Individual Alcian Blue Areas and Cartilage Cells (Paraffin, Alcian-PAS), 125X.

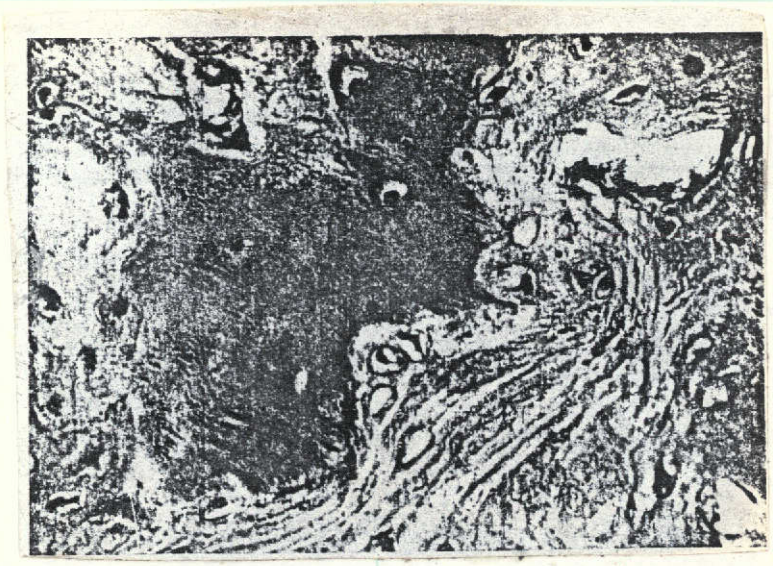


Figure 22. Highly Metachromatic Cartilage Ground Substance Remains, Swollen Cartilage Cells With Increased Increased Basophilia of the Cartilage Capsule and Direct Cell Environment (Paraffin, Toduidine Blue), 500X.

The joint fissure has already been destroyed, and in addition to the remains /237 of cartilage cells and cartilage ground substance, there are also extensive areas of necrosis. Processes extend from the marrow space of the subchondral spongiosa in the direction of the central necrosis (Figure 23). These extensions consist of blood bessels and the endothelial and mesenchymal cells accompanying them, which become preosteoblasts and osteoblasts. Vascular extensions merge with those from other marrow areas, branch out and pass through newly formed bone tissue to an increasing degree toward the central areas of necrosis from both chondyles, until they form a ossal fusion at several points simultaneously.

The vascular sprouts are reminiscent of the so-called "bore heads" [Bohrkoefe] demonstrated by Schenk et al., except that despite improved technology with decalcified bone thin sections after acrylate embedding, osteoclasts could not be detected at the tip (Figure 24).

On the other hand, the acrylate technique did allow the study of a form of ossification whose principal elements constitute blood vessels and osteoblasts closely linked with these vessels (Figure 25). The preliminary stages of the

osteoblasts are vascular endothelium or endothelial tubes accompanied by undifferentiated mesenchymal cells (Figure 26). As a result of this ossification /239
process, osteocytes are observed which lie in the bone ground substance which they produce in the osteoblast stage. These processes occur in the former meniscus area without any of the tissue components originating in the meniscus (collagen fiber bundles or cartilage cells) being detectable. In ary case, with connective tissue stains, it is possible to pick up fine fiber threads between the vessels and the osteoblasts, so that the existing mode of ossification is most reminiscent of a transitional form between the former and the primarily angiogenic ossification according to Krompecher (Figure 27).

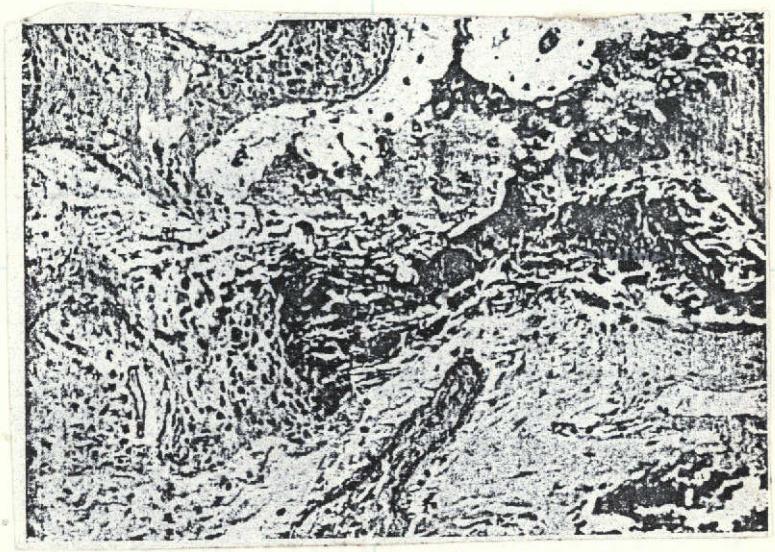


Figure 23. Central Necroses and Cartilage Cell Remains in the Pressure /238
Zone Area. Penetration of Germinating Extensions From the Subchondral Marrow Space, Consisting of a Central Vessel, Endothelial and Mesenchymal Cells (Methylmethacrylate, Giemsa), 125X.

Application of Individual Criteria to the Immobilization Times and Spring Forces

Following discussion of the individual criteria, we will now apply the findings that were made to the immobilization times and the various amounts of spring force that were applied (table).

From a comparision of the immobilization times and the spring forces used, the following developments can be found on the basis of modification and fusion of the joint.

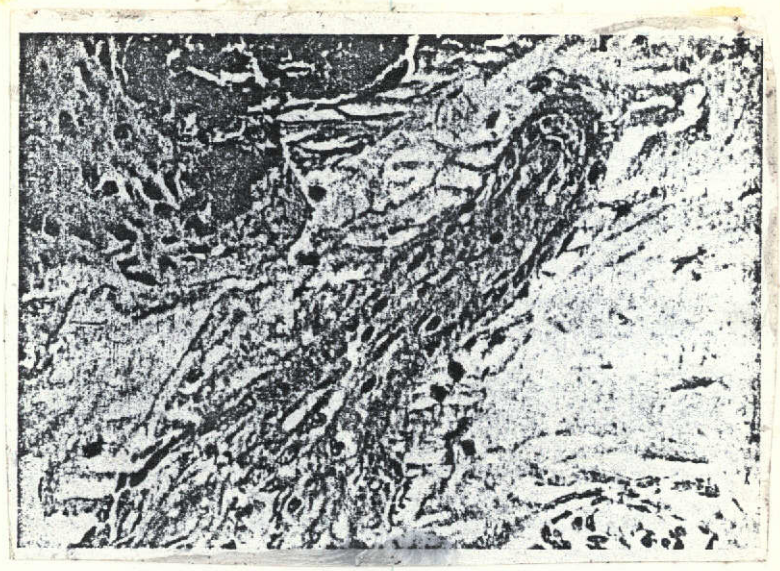


Figure 24. Section of Figure 23.

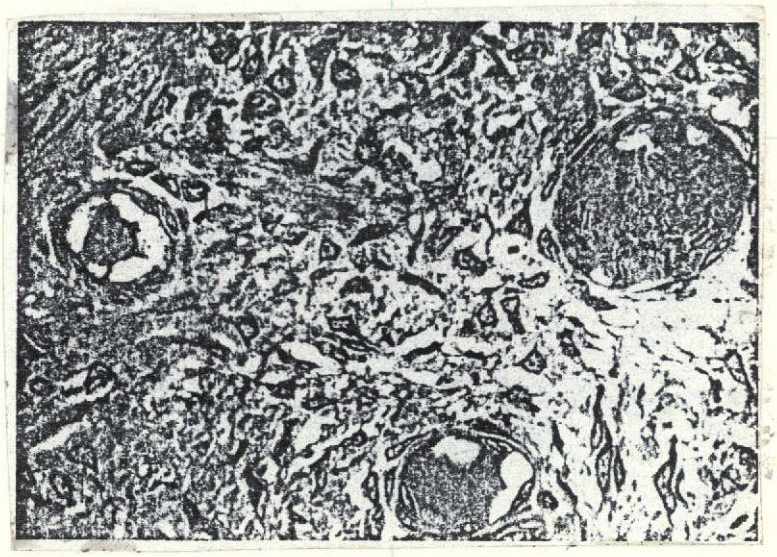


Figure 25. Stepwise Conversion of the Vascular Endothilia Occurring in the Vascular Walls in Preosteoblasts and Osteoblasts (Methylmethacrylate, Giemas), 500X.

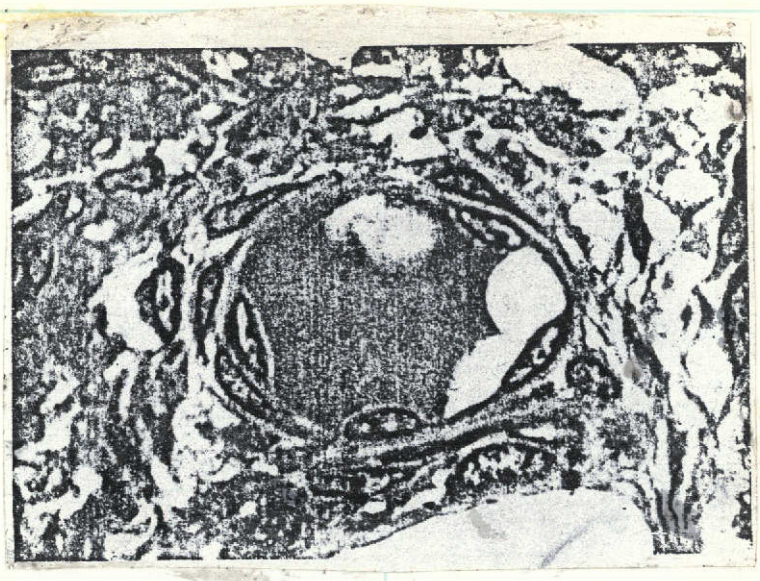


Figure 26. Section of Figure 25.

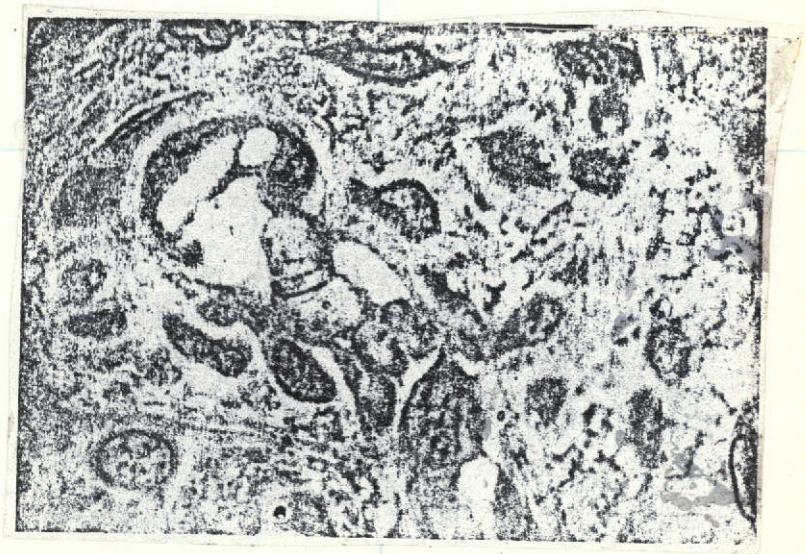


Figure 27. Stepwise Development of Preosteoblasts and Osteoblasts From Vascular Endothilia. (Methylmethacrylate, Ladewig), 500X.

/240

The table shows the gradual development of cartilage degeneration as a function of pressure. The appearance of atypical chondrones is an occasional observation, but apparently does not appear at all immobilization times.

Changes do not always take place in the cartilage. At higher spring forces earlier reconstruction of the cartilage was observed earlier.

Table: Arrangement of Individual Criteria for Immobilization Times and Spring Forces.

Time (month)	Spring force (p)																								
	Group I: 4,000 to 10,000							Group II: 12,000 to 16,000								Group III: 18,000 to 24,000									
½	A_I	A_{II}						A_I	A_{II}							A_I	A_{II}	A_{III}							
1	A_I	A_{II}		B				A_I	A_{II}	A_{III}	B					A_I	A_{II}	A_{III}	B						
2	A_I	A_{II}	A_{III}	B		D	E	A_I	A_{II}	A_{III}	B	C	D	E		A_I	A_{II}	A_{III}	B	C		E			
3	A_I	A_{II}	A_{III}	B	C	D	E	A_I	A_{II}	A_{III}			D	E		A_I	A_{II}	A_{III}	B			E			
6	A_I	A_{II}	A_{III}		C			F	A_I	A_{II}	A_{III}		C		E	F	A_I	A_{II}	A_{III}	B	C		E	F	

Arrangement of the Findings by Spring Forces and Immobilization Times: Cartilage degeneration A_I, A_{II}, A_{III}, atypical chondrones B, Cartilage Reconstruction C, Fibrous Cartilage D, Local Hyperostosis E, Joint Fusion F.

The striking absence of cartilage fibers in the third group is striking: possibly the intraarticular pressure is too high for the formation of fibrous cartilage.

The appearance of local hyperostosis beneath the pressure zone is an observation that was always made with one exception, but it always developed only after two months had elapsed.

The bony modifications in the joint began six months after the start of the test at the earliest. It occurred in the first group in one out of six animals in the third group.

A fourth group served as controls. In this group, the bolts were inserted transarticularly only and a spring was implanted simultaneously, but the latter was not compressed.

In this group, half the animals showed a slight oscillating mobility of the joint at the end of the test. The pressure bolts had loosened, and the bores for the pressure bolts had become wider and showed a lining of connective tissue. The most striking thing about this group was the fact that ossal joint ankylosis did not occur even after six months of immobilization.

Strikingly, there was also cartilage degeneration, but up to two months after the beginning of the experiment, cartilage degeneration could only be seen in Stage I, after which (therefore for immobilization times of three and

six months) there was cartilage degeneration in Stage II. After three and six months, atypical chondrones were observed.

Another control group consisted of one animal for each immobilization time, in which there was only an amputation of the shin. These animals placed no stress upon their extremities, but definitely did move about. The microscopic investigation of these joints showed no significant changes aside from a narrowing of the joint cartilage.

Discussion

Pressure Stress on Joint

For an interpretation of the findings obtained, it is important to know the original mechanical conditions in advance.

The continuation of absolute immobilization of the joint was checked during the current test and in the preparation of the joint, and the action of frictional forces and pressure in combination with incomplete immobilization was therefore excluded.

The compressed spring force was known at all times and showed a decrease in force described by stretching the spring 25% after two weeks and 50% after four weeks, with a largely constant value. The fact of stretching of the spring provides various topics for discussion: elastic cartilage deformation, loss of fluid and cartilage pressure necrosis led rapidly to a narrowing of the joint fissure; the tibia head and femur chondyles came closer together. Both at the head of the bolt and beneath the cutting cap of the spring, the x-ray picture after 14 days showed regular symptoms of slight ossal resorption. These resorption phenomena should probably be interpreted as pressure necrosis, which occurred to different degrees in all animals, corresponding to the forces acting upon them. Finally, the flattening of the femur chondyles led to further stretching of the springs.

To determine the actual compressive forces, it was necessary to determine the size of the pressure application zone in the cartilage contact area.

Measurements with a loupe provide only an approximate value and also show the state only at the end of the experiment, as it has developed as the consequence of mechanical affects. This development, both with increasing compressive force and also with increasing duration, necessarily leads to a constant increase in the size of the cartilage contact zone, so that at high spring force after a long experiment larger pressure marks can be found than after a shorter experiment at low force. Likewise, the examination of the pressure bearing zones with a loupe shows 14 mm^2 = 1/7 cm^2 to 32 mm^2 = 1/3 cm^2. The constant increase in area of the contact zones can be attributed to elastic deformation, cartilage pressure necrosis and flattening of the femur chondyles.

These considerations show that the cartilage pressure, as a quotient of force per area, even at the beginning of the experiment has no linear dependence upon the measured spring force, and that the cartilage pressure during the course of the experiment, especially in Group III with high spring values, decreases still more markedly than the spring force. The actual cartilage pressure values therefore had largely reached uniform value in all three experimental groups after four weeks, which was tolerated by the tissue, so that the critical differences in the mechanical effects were manifested during the initial period. The differences can be seen from a comparison of the findings of Groups I - III, and the frequency of ossal fusion in Group III is striking.

If we assume for the sake of simplification that the cartilage contact zones are congruent surfaces, which fit closely together, we can calculate the following pressure values for the three groups from the spring force and the area:

Group I up to 50 kp per square centimeter; /243
Group II up to 90 kp per square centimeter;
Group III up to 120 kp per square centimeter;

If we compare the calculated pressure values with the figures that were obtained in checking the mechanical characteristics of various cartilages from the physical-technical viewpoint, it becomes clear that the compression of the joints at high spring forces, as in Group III, constitutes a powerful intervention in the joint fissure, which reaches or exceeds the limits of mechanical

tolerance. The maximum applied compression corresponds to a weight application of 25 kilograms!

Goecke, in elasticity studies on young and old joint cartilage in man, found a fracture limit between 50 and 115 kp/cm^2 for cartilage from the knee joint.

Still earlier, Baer in his elasticity tests on cartilage found an irreversible change in elastic behavior with a prolonged load of 7 km/cm^2. Intermitted stressing at much higher forces with rapid alternation produced no corresponding changes.

Bargmann cites the compressive strength of the rib cartilage in man at 150 kp/cm^2; Camosso and Marotti, in material tests with joint cartilage from cattle of various ages found fracture values between 200 kp/cm^2 in young animals and 600 km/cm^2 in old animals.

According to Steindler, cartilage is perfectly elastic if a pressure load of up to 12 kp acts for no longer than one hour.

If we assume (for example, in the case of Group III with spring forces of 18 to 24) that the pressure zone area is between 1/5th and 1/3rd cm^2, we can calculate compression values between 54 and 120 kp/cm^2. These values reach the limit of mechanical tolerance, as given by Bargmann and especially by Goecke.

Complete necrosis of the cartilage in the contact area occurs in Group I after two months, in group II after one month and in Group III after only 14 days. The reason for this can be found in the difference shown in the effective compression pressures.

For Group III, we must assume that the spring forces of 20 to 24 kp involve direct mechanical cartilage destruction. This is also indicated by the presence of compressed, necrotic cartilage remains in the background of the pressure marks. In Group II, with spring forces of 12 to 16 kp, we must also assume that some animals suffered direct mechanical cartilage destruction, but this does not suffice to destroy the cartilage rapidly through its entire thickness. Hence, there must be other mechanisms which are significant as far as destruction of cartilage is concerned.

Immobilization of the joints and additional compression cause a disturbance of blood and synovial circulation in the various parts of the joints and influence nourishment and metabolism in an unsatisfactory fashing (Hodge and McKibbin; Homdhal and Ingelmark). Holth and Westerborn as well as Matthias and Gluppe were able to show that joint immobilization alone rapidly leads to a definite reduction of cartilage thickness, which can be attributed to rapid loss of fluid. Titze and Leb showed changes in the resorptive function of the synovial membrane following immobilization of joints by transfixation. Later spreading of the connective tissue joint pannus obliterates the joint fissure and the synovia eventually disappears completely. However earlier in the compressed cartilage contact area diffusion disturbances occur which accelerate the development of cartilage pressure necrosis.

Disturbances in nourishment of this kind are seen as the consequence of immobilization and compression, particularly for Group I, spring forces of 4 to 10 km, as the cause of slow development of cartilage pressure necrosis.

Salter and Field in their experiments found initial symptions of destruction /244 of tissue after three to six days; Crelin and Southwick saw the first pressure necroses of cartilage after six days. Both groups of authors during this time, prior to the development of the first visible symptoms of catabiosis, an indication that under their experimental conditions it was not direct mechanical cartilage destruction which took place but pressure-induced disturbance of nourishment which led to destruction of cartilage.

In our experimental series, the active mechanism which leads to cartilage pressure necrosis in the immobilization and compression of a joint proved the following:

Group I: compressive force of 4 to 10 kp, low pressure value, effective mechanism predominantly nourishment and metabolism disturbance.

Group II: compressive force of 12 to 16 kp, average pressure values, effective mechanism partila disturbance of nourishment, partially mechanical destruction.

Group III: spring force of 18 to 24 kp, high pressure values, effective mechanism primarily mechanical destruction.

Bony Reconstruction of Joint

Preliminary tests on the type of immobilization show that complete immobilization is possible only through internal fixation.

It also has the striking advantage that following primary healing of the wounds secondary infection by projecting osteosynthetic material can be prevented relaibly. Plaster casts, which always pose special problems in animals with their conically shaped extremities, are unnecessary.

Our own experiments with transarticular position of specially constructed pressure bolts with rectangular positioning of the rabbit knee joint and simultaneous amputation of the shin, guarantee an absolute resting position with exclusion of body weight; it simultaneously allows measured pressure loading even at longer immobilization times.

The immobilization of the knee joint of the rabbit with constant compression after six months in some of the animals led to ossal fusion of the joint.

A total of 15 joints were compressed with defferent spring forces for six months, and six joints showed ossal fusion of the joint fissure after this period of time. There was a definite relationship between ossal fusion and compressive force, for in six animals with maximum spring forces of 20 to 24 kp there were five cases of ossal ankylosis, while all weaker spring forces in only two cases out of 9 led to ossal fusion. The control animals with "immobilization without pressure" also failed to show any complete disappearance of cartilage after six months, either in the cartilage contact area or outside the front.

According to Kuntscher, a joint which has had a nail driven through it and is therefore absolutely stabilized is astonishingly mobile, even years after the nail has been pulled out as he himself puts it. The pure immobilization by internal fixation therefore leads only to functional and not anatomic stiffening.

Likewise, Schneider produced arthrodesis in the rabbit, by multiple intraarticular injections of a proteolytic enzyme (papain) with subsequent immobilization of the joint for eight weeks. After this period of time, he

found that 67% of his animals display ossal ankylosis, and fusion had begun in 70% of the control animals whose joints were operatively decartilagized and filled with autogenic bone chips.

The bridging bones in Schneider developed by maturation of dense connective tissue to form a fibrous cartilagenous callus and finally bone.

Therefore Schneider was able to prove that with absolute immobilization /245
in animal experiments a joint can fuse. In the experiments of Schneider, it was absolute immobilization which led to ossal fusion but only after enzymatic menas had been used to destroy the cartilage beforehand, with injections of papain.

In our own experiments, the question arose of whether measured amounts of pressure with complete immobilization would be able to accomplish what Schneider did enzymatically, namely, destroy cartilage, in order to bring the subchondral bone into contact with the subchondral bones on the opposite side.

In part, there was preliminary destruction of cartilage which could be seen in the pressure zone area as a function of the level of pressure; the prerequisite for ossal fusion, on the other hand, was reconstruction of the cartilage, i.e., ossal replacement of the cartilage in the course of a sort of enchondral ossification, the fusion of the joint.

Operative decartilagization as well as enzymatic-chemical destruction of the cartilage, assuming complete immobilization, led to ossal joint ankylosis. Immobilization alone, even if absolute, did not lead to ankylosis. Ankylosis could be achieved, however, if compression of the joint was employed for absolute immobilization, but, only if the compression exceeded the mechanical stress limit of the cartilage. If the compressive forces were less, there were mulitple reconstruction processes in all the tissue of the joint, but there was no ossal joint ankylosis in a comparable time.

Strikingly, reconstruction of the joint after spring compression often began not at the center of pressure effect, but at the edges of the pressure mark. In this area, beginning in the marrow space, there was a continuous reconstruction of the joint. As the vessel penetrated, there was initial

ossal replacement of the joint cartilage; then the adjacent meniscus area became involved in the ossification process, with the cells of the meniscus tissue behaving essentially as hyaline cartilage cells within the scope of the enchondral ossification mode.

The ossal joint fissure fusion therefore corresponded in its development to enchondral ossification in the growth of cartilagenous performed skeletal parts.

In addition to the type of ossification discussed, which is reminiscent of enchondral ossification, there was a type of ossification which involved predominance of vessels, osteoblasts and osteocytes and was reminiscent of the primarily angiogenic ossification according to Krompecher.

The simultaneous appearance of fibrous structures indicates, however, that it is a mixed form with desmoid ossification which is involved. This primarily angiogenic type of ossification since Krompecher's time has been observed recently by the Swiss work group surrounding Robert Schenk (but in the corticalis, in the course of so-called primary bone healing).

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